II. Remarks

A. Status of the Claims

Claims 1-4, 6-20 and 26-31 will be pending after entry of this amendment. Claims 1, 3, 4, 9 and 15 have been amended without prejudice. Independent claims 26 and 27 and dependent claims 28-31 are newly added. Support for the amendments and new claims can be found in the specification as originally filed, e.g., at paragraphs [0038]-[0042]; [0060]; [0078]; [0098] and the originally filed claims. Applicant respectfully submits that no new matter has been added by virtue of this amendment.

The Examiner's indication that claims 4-7, 9, 10, 14, 17-20 and 25 are allowable except for being dependent on a rejected base claims is acknowledged with appreciation. The limitations of claims 6, 7, 9, 10, 14 and 18-20 have been incorporated into new independent claim 27.

B. Statement of Substance of Interview

The Applicant appreciates the courtesies extended by the Examiner during the telephone interview of April 7, 2009. During the interview, WO 95/28171 was discussed as well as proposed to the independent claims, including limiting claim 1 to certain disease states of original claim 15.

The Examiner indicated that the inclusion of certain disease states from claim 15 appeared to overcome the cited rejection but that the proposed amendments would need to be further reviewed in view of the prior art. The examiner indicated that the claims may still be rejected under obviousness if the mechanisms of disease conditions of the instant claims are sufficiently similar to those taught by the prior art.

The Examiner also indicated that the administration of certain claimed administration methods may also obviate the rejections.

C. Claim Rejections under 35 U.S.C. § 102(b)

In the Office Action, claims 1-3, 8, 11-13, 15 and 16 were rejected under 35 U.S.C. § 102(b) as being anticipated by WO95/28171 to Sanders et al. (the '171 Application). The Examiner stated that "[s]ince the scope of the claims is drawn to a method of blocking or reducing physiological reactions and not to actual blocking of IgE antibodies binding with antigen, Sanders et al teach the claimed methods in that then reference teaches controlling at least one symptom of rhinorrhea, otitis media, excessive salivation, asthma, COPD, excessive stomach acid secretion, spastic colitis or excessive sweating in mammals, including humans."

In response, the present claims have been amended without prejudice to include disease states that are not included in the '171 Application, namely, allergic rhinitis (independent claims 1 and 27) and allergic dermatitis (independent claim 26). Further, in response to the Examiner's Interview Summary of April 9, 2009, the discussion below and the attached Declaration of the inventor, Dr. Ira Sanders under 37 C.F.R. §1.132, will address the Applicant's position that the mechanism of disease conditions of the instant claims are not similar to those taught by the prior art.

The '171 Application

The '171 Application is directed to treating the condition of vasomotor rhinitis (see, e.g., page 2, lines 8-11; lines 33-35; page 14, lines 2-4 of the '171 Application) which is a distinct condition from allergic rhinitis as recited in the present claims. *Declaration of Ira Sanders* ¶ 7 (attached as Appendix 1).

Vasomotor rhinitis is a simple and relatively uncommon condition believed caused by overactivity of cholinergic nerves innervating a subset of nasal glands to produce a thin watery secretion. As stated in an authoritative source, "...vasomotor rhinitis occurs in some elderly people who experience a dripping, watery rhinorrhea that becomes pronounced at mealtime but may be persistently present in many daily activities. There is little sneezing, pruritis, congestion,

or lower respiratory tract symptoms associated with this entity. Eosinophils are not present in nasal secretions. Treatment with most medications including antihistamine/decongestants, cromolyn sodium, and topical steroids are usually not effective..."[1] *Id.* ¶8.

In sharp contrast, allergic rhinitis is caused by a distinct mechanism from that of vasomotor rhinitis. The primary source of fluid in allergic rhinitis is from vasodilation and increased permeability of nasal blood vessels. This allows fluid to "leak" directly from blood vessels into the nasal cavity. A secondary mechanism is that the neurohumors released from immune cells directly stimulate mucous secreting cells. *Id.* ¶9

Vasomotor rhinitis is limited to a watery rhinorrhea and caused by eating or temperature change (see page 11, lines 18-22 of the present application). In contrast to vasomotor rhinitis, allergic rhinitis is associated with:

(i) the release of histamine, heparin and neuropeptides which in turn cause vessels to dilate and congest the nose, or bypass nerves to directly stimulate mucus production as well as cause reflex mucus production, increased cilia movement, nasal congestion and sneezing (see page 9, lines 10-14 of the present application);

(ii) mast cell degranulation with reflex mucous production, increased cilia movement and sneezing (see page 7, line 30 to page 8, line 2 of the present application);

(iii) the release of nerve growth factor from mast cells and eosinophils, thereby resulting in growth of nasal sensory nerves and increased hyperactivity which makes the patient more susceptible to viral and bacterial infections. In addition allergies cause qualitative changes in nerve reflexes such that they are activated more easily by both allergic and non-allergic stimuli (see page 8, lines 10-21 of the present application). *Id.* ¶10.

To further evidence the distinct mechanisms of vasomotor rhinitis and allergic rhinitis, Dr. Sanders' notes that vasomotor rhinitis is treated with drugs that block acetylcholine, while

[1] Immunology and Allergy Clinics of North America, Fahey J and Fauci A, eds. Volume 7, Issue 1, Upper Respiratory Disorders, chapter, NonAllergic Chronic Rhinitis Syndromes, Jocobs, R, pages 93-104 (Attached as Appendix 2) Exhibit.

allergic rhinitis is treated with desensitization, anti-histamines and steroids. The drugs used for allergic rhinitis are not therapeutically effective on vasomotor rhinitis (as paragraph 8 above). This is because the mechanism of vasomotor rhinitis appears to involve only a small group of cholinergic nerves innervating the nasal glands that produce a watery secretion with low content of mucus. In contrast, allergic rhinitis involves many different cell types including B-cells, T-cells, macrophages, basophils, mast cells, eosinophils, as well as sensory and non-cholinergic nerves. The mediators that are involved in allergic rhinitis are extremely varied and include: histamine, tryptase, chymase, kinins, heparin, leukotrienes, prostaglandins, eosinophilic basic protein, nerve growth factor and many others. *Id.* ¶11.

In contrast to the treatment of vasomotor rhinitis, treatment of allergic rhinitis according to the present claims presents the following properties:

-decreased release of histamine, heparin and neuropeptides;
-decreased rhinorrhea from permeable nasal blood vessels, from direct stimulation of mucus glands by neurohumors, and from reflex mucus production;
-decreased nasal congestion and sneezing. *Id.* ¶12.

The '171 Application is specific to the nerves that use acetylcholine as their neurotransmitter, and the possibility of blocking other neurotransmitters or neuropeptides is rejected by the interpretation therein of the prior scientific literature (see page 2, lines 25-29 of the '171 Application), the results of the salivation experiment described in the specification (see page 11, line 26-29 of the '171 Application), as well as the rhinorrhea experiments (see page 18 line 25-28 and page 19, lines 17 to 21 of the '171 Application). *Id.* ¶13.

The term "rhinorrhea" means excess nasal secretion and the term is applied to a variety of other conditions. For example, cerebrospinal fluid (CSF) rhinorrhea occurs when there is a skull fracture and CSF leaks from the central nervous system out of the nose. Another example is the purulent (pus) rhinorrhea resulting from an acute sinus infection. In view of the disclosure of the treatment of vasomotor rhinorrhea in the '171 Application, it is Dr. Sanders' opinion that no practitioner of ordinary skill in the art would generalize that any rhinorrhea such as CNS rhinorrhea or purulent rhinorrhea could be blocked by neurotoxins. Similarly, it is Dr. Sanders'

opinion that in view of the '171 Application, a practitioner of ordinary skill in the art would not have any expectation of success that allergic rhinorrhea could be blocked by neurotoxins as recited in the present claims. *Id.* ¶14.

To further evidence the distinct mechanisms of vasomotor rhinitis and allergic rhinitis, Dr. Sanders notes that the only surgical treatment for vasomotor rhinitis is to cut the nerves innervating the nose (Vidian neurectomy). This is never done and would not be effective for allergic rhinitis. Rather, surgeries for allergic rhinitis treat the long term changes of mucosal thickening, nasal polyps and recurring sinus infections. *Id.* ¶15.

Allergic dermatitis is also caused by allergic pathways as discussed above and in Dr. Sanders opinion, independent claim 26, directed to treating allergic dermatitis is also not anticipated or obvious from the '171 Application. *Id.* ¶16.

In view of the amendments made and positions taken, the Examiner is respectfully requested to remove the rejections of the pending claims over the '171 Application.

D. Claim Rejections under 35 U.S.C. § 112

In the Office Action, claims 4-7, 9, 10, 14, 17-20 and 25 were rejected on the grounds of being indefinite for being dependent on a rejected base claim.

In view of the discussion above, Applicants respectfully submit that these claims are now dependent on allowable claims and the Examiner is respectfully requested to remove the indefinite rejections.

Further independent claim 27 incorporates the unique administration methods of claims 6, 7, 9, 10, 14 and 18-20 which were not included in the prior art rejections in the February 4, 2009 Office Action. In the opinion of Dr. Sanders, these claims are also not obvious in view of the '171 Application due to the recitation of the administration methods. *Id.* ¶17.

III. Conclusion

In view of the amendments made and arguments presented, it is believed that all claims are in condition for allowance. If the Examiner believes that issues may be resolved by a telephone interview, the Examiner is invited to telephone the undersigned at (973)597-2404. The undersigned also may be contacted via e-mail at rparadiso@lowenstein.com. All correspondence should be directed to our address listed below.

AUTHORIZATION

The Commissioner is hereby authorized to charge any fees that may be required, or credit any overpayment, to Deposit Account No. 50-1358.

Respectfully submitted,
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